



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/GB93/02367 <b>(22) International Filing Date:</b> 17 November 1993 (17.11.93)  <b>(30) Priority data:</b> <table border="0"> <tr> <td>9224057.1 ✓</td> <td>17 November 1992 (17.11.92)</td> <td>GB</td> </tr> <tr> <td>9304677.9 ✓</td> <td>8 March 1993 (08.03.93)</td> <td>GB</td> </tr> <tr> <td>9304680.3 ✓</td> <td>8 March 1993 (08.03.93)</td> <td>GB</td> </tr> <tr> <td>9311047.6 ✓</td> <td>28 May 1993 (28.05.93)</td> <td>GB</td> </tr> <tr> <td>9313763.6 ✓</td> <td>2 July 1993 (02.07.93)</td> <td>GB</td> </tr> <tr> <td>9316099.2 ✓</td> <td>3 August 1993 (03.08.93)</td> <td>GB</td> </tr> <tr> <td>9321344.5 ✓</td> <td>15 October 1993 (15.10.93)</td> <td>GB</td> </tr> </table> <b>(71) Applicant (for all designated States except US):</b> LUDWIG INSTITUTE FOR CANCER RESEARCH [GB/GB]; St. Mary's Hospital Medical School, Norfolk Place, Paddington, London W2 1PG (GB).		9224057.1 ✓	17 November 1992 (17.11.92)	GB	9304677.9 ✓	8 March 1993 (08.03.93)	GB	9304680.3 ✓	8 March 1993 (08.03.93)	GB	9311047.6 ✓	28 May 1993 (28.05.93)	GB	9313763.6 ✓	2 July 1993 (02.07.93)	GB	9316099.2 ✓	3 August 1993 (03.08.93)	GB	9321344.5 ✓	15 October 1993 (15.10.93)	GB	<b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> MIYAZONO, Kohei [JP/SE]; Flogstavägen 63D, S-752 63 Uppsala (SE). DIJKE, Peter, Ten [NL/SE]; Flogstavägen 25C, S-752 63 Uppsala (SE). FRANZEN, Petra [SE/SE]; Lindsbergsgatan 15b, S-752 40 Uppsala (SE). YAMASHITA, Hidetoshi [JP/SE]; Flogstavägen 33A, S-752 63 Uppsala (SE). HELDIN, Carl-Henrik [SE/SE]; Hesselmans väg 35, S-752 63 Uppsala (SE).  <b>(74) Agent:</b> GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).  <b>(81) Designated States:</b> AU, CA, JP, KR, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
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**(54) Title:** ACTIVIN RECEPTOR-LIKE KINASES, PROTEINS HAVING SERINE THREONINE KINASE DOMAINS AND THEIR USE

cons.aa	C C G V	A K	E
HTGFBR-II	LDTLVGKGRFAEYVYKQJLKHQTSQFETVAVKI	FFYDHYASWDRKD	IFSDINLGHENLLOF
BACTR-IIIB	LLEIKARGRFCCVWKAQLN	-----DFVAVKI	KPLQOKQSWQSEREIFSTPGQGHENLLOF
BACTR-II	LLEVKARGRFCCVWKAQLN	-----ETVAVKI	FFIQOKQSWQNEYEVYSIPQGHENLLOF
daf-1	LKRVGSGRPFQVSRGQYRG	-----EAVAVKVTAID	DEPAFKEIETIFETRLRHPVRLY
subdomains	I	II	III IV

HTGFBR-II	LTAERKTELCKQVWMLITAFHAKGNLQEYLTRHVISWEDLRVGSGLAGLSHLHSDHTP-C
BACTR-IIIB	IAAEKRGSNLEVLMLITAFHAKGNLQEYLTRHVISWEDLRVGSGLAGLSHLHSDHTP-C
BACTR-II	IGAEKRGTSVDVDMMLITAFHAKGNLQEYLTRHVISWEDLRVGSGLAGLSHLHSDHTP-C
daf-1	IGSDRVDTGPFVTEMLVITEHPSGSLHDFLENTVNIETTYNLMRSTASGLAFHMQIGGSK
subdomains	V VI-A

cons.aa	DLK N	DFG
HTGFBR-II	-GRPKPIVHVDLSSNLLVNDLTCCLCDFGLSLRL	---GPYSSVDDLANSQGVGTARYTHAP
BACTR-IIIB	CEGKQPSIAHVDLSSNLLVNDLTCCLCDFGLSLRL	---EPGKPPGD---THGQVGTARYTHAP
BACTR-II	-DGKQPAISHVDLSSNLLVNDLTCCLCDFGLSLRL	---BAGKSGD---THGQVGTARYTHAP
daf-1	-ESNKPAPVHVDLSSNLLVNDLTCCLCDFGLSLRL	---ENYKCGTVRYTHAP
subdomains	VI-B VII	VIII

**(57) Abstract**

A new receptor family has been identified, of activin-like kinases. Novel proteins have activin/TGF- $\beta$ -type I receptor functionality, and have consequential diagnostic/therapeutic utility. They may have a serine/threonine kinase domain, a DFKSRN or DLKSKN sequence in subdomain VIB and/or a GTKRYM sequence in subdomain VIII.

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